REMARKS

The Applicant respectfully requests reconsideration of the rejections of the claims and the objection to the drawings made in the Final Office Action dated September 23, 2005.

Rejection Under 35 USC 112

In the Final Office Action dated September 23, 2005, all claims were rejected under 35 USC 112. That Office Action stated:

> [T]here is NO mention in the specification about a first set of pellets and a second set of pellets contained *upon a structure*. The specification describes individual pellets with individual coatings upon a structure in single form (being thick or thin) but nowhere does the specification disclose the arrangement of these pellets as a first set and second set upon *a structure* as claimed.

Office Action dated September 23, 2005, page 2 (emphasis in original).

With respect to this rejection, the Applicant respectfully submits the following comments and respectfully requests that the Examiner kindly reconsider this ground of rejection.

Specifically, the Applicant respectfully submits that a person of ordinary skill in the art, reading the original disclosure as a whole, would recognize that the disclosure does disclose different sets of pellets with different coatings (thick and thin) on a single structure.

First, the Abstract of the Disclosure states that the invention relates to coating a **single** structure – such as a "medical device structure" (like "a stent") – with a plurality of pellets having **different** release rates:

> The invention relates to a method and device for coating **a device** with time- release drugs by providing a plurality of micro coated pellets having **different release rates** on **the surface of the medical device structure, e.g., a stent**. Organizing the micro pellets with **different release rates** on **the structure** can result in

> the structure having a plurality of release regions with varying release profiles.

Abstract (emphasis added).

Second, the Detailed Description and associated Figures describe and illustrate an embodiment in FIG. 1 in which a **single** structure is shown with four **different** sets of coated pellets 130, 140, 150 and 160:

> FIG. 1 is a schematic representation of one embodiment of the invention. Referring to FIG. 1, an enlarged segment 100 represents a portion of **a medical device structure**, e.g., a stent strut 110, having deposited thereon an adhesive layer 120. **Micro coated pellets 130, 140, 150 and 160** are embedded in adhesive layer 120 and are bonded to stent strut 110. Although not shown, each of the micro coated pellets 130, 140, 150 and 160 is represented as having a **different** composition and/or dissolution (decomposition) rate.

Specification, para. 18 (emphasis added).

Third, the Specification expressly states that the sets of micro coated pellets 130, 140, 150 and 160 can be arranged, for example, in columns or rows on the device:

> The micro coated pellets can be arranged according to their expected release profile or decomposition rate. For example, assuming that micro pellets 130, 140, 150 and 160 have different release profiles, they can be arranged on the structure 110 such that micro coated pellets having a substantially similar release profile are not immediately adjacent to each other. In this embodiment, the surface of the structure can be coated to have micro pellets 130 placed along the longitudinal axis of the stent and in a **columnar** arrangement. With this arrangement, repeating columns of micro coated pellets 130 are adjacent to, for example, columns of micro coated pellets 140 and 160. A similar arrangement can be implemented **circumferentially** around the periphery of the stent. In this embodiment, repeating **rows** of micro coated pellets 130 appear as rings around the circumference of the stent.

Specification, para. 23 (emphasis added). Thus, in FIG. 1, each pellet can represent a row or column of pellets extending in a plane perpendicular to the plane of the drawing. Alternatively, the regions where each set of pellets is deposited "can be discontiguous and/or disconnected." Specification, para. 12.

Fourth, the Detailed Description and associated Figures go on to describe details of examples of pellets that may be used on a structure as shown in FIG. 1. The Detailed Description explains that the pellets can be given different release rates by changing the "**thickness** of the micro coating layer":

> FIG. 2 is a schematic representation of an exemplary micro coated pellet. ... **[T]he thickness of the micro coating layer 220 can affect the drug release profile. A thicker polymer coating layer would lead to a slower dissolution than a thinner polymer layer of the same composition.**

Specification, para. 27 (emphasis added).

Fifth, similar to the Abstract and Summary of Invention, the Detailed Description states that "multiple micro coated pellets with different dissolution rates can be placed along a segment of a structure":

> **Thus, multiple micro coated pellets with different dissolution rates can be placed along a segment of a structure** to provide a device with pre-defined time-release characteristics.

Specification, para. 28 (emphasis added).

Sixth, the Summary of the Invention states that the pellets with the "different release rates" (as stated in the Abstract) can be "**similar**" in "**size**":

> In another embodiment, each site [on the structure] can have the form of a micro coated pellet (or coated pellets) with each coated pellet including at least one active substance. . . . The coated

> pellets can be **similar** or dissimilar in composition, **size**, release rate or decomposition rate.

Specification, para. 11 (emphasis added).

Seventh, the Specification makes clear that this similarity of size of the pellets on the structure may be maintained even when the coating thicknesses are different. FIGS. 3A-3D illustrate this. FIGS. 3A-D show four different pellets A-D that can be used on a structure similar to the four different pellets illustrated in FIG. 1. Each of the pellets A-D in FIGS. 3A-3D is illustrated as having substantially the same size as each other. Each pellet A-D has a **different** coating thickness but the same amount of drug. To keep the pellets A-D all substantially the same size, the pellets A-D have **different** amounts of placebo. This is described in paragraphs 30-33 of the Specification. The following chart shows the details of the examples of pellets A-D that are described in paragraphs 30-33 of the Specification:

Pellet	Amount of Drug/Placebo Mixture (M)	Percentage Drug in Mixture (%D)	Percentage Placebo in Mixture (%P)	Amount of Drug (M * %D)	Amount of Placebo (M * %P)
A	8 µg	25%	75%	2 µg (= 8*.25)	6 µg (= 8*.75)
B	4 µg	50%	50%	2 µg (= 4*.50)	2 µg (= 4*.50)
C	2.5 µg	80%	20%	2.0 µg (= 2.5*.80)	0.5 µg (=2.5 * .20)
D	2 µg	100%	0%	2 µg (=2 *1.0)	0 µg (=0*1.0)

Because the pellet sets A-D have different coating thicknesses but the same drug amounts, keeping all of the pellets substantially the same size means that there will be extra internal volume in the pellets with thinner coatings. The Specification thus describes the use of placebo to fill this extra volume:

> Since the **internal volume** of the micro coated pellet represented in FIG. 3A is **larger** than the micro coated pellet represented in FIG. 3B, the drug mixture of FIG. 3A can contain **more placebo** in order to ensure that the drug content of the micro coated pellet of FIG. 3A would amount to 2 μg.
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> * * *
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> Furthermore, since the **internal volume** of the pellet of FIG. 3C is **smaller** than those of Figs. 3A or 3B, the drug mixture of pellet of FIG. 3C may contain **less placebo** than each of the pellets 3A or 3B in order to have the drug content be 2μg, as will the others.
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> * * *
>
> **To keep the micro coated pellets at substantially the same size,** the pellets with the fastest release rate can contain some **inert chemical [or placebo]**, such as mannitol. If the pellets having the faster release rate are supplied with a thinner micro coating, the addition of an inert compound would serve to increase the volume of the pellet while keeping the drug content constant.

Specification, paras. 31, 33, 40 (emphasis added).

Eighth, the Specification makes clear that the pellets A-D are used together on the same structure, as shown in FIG. 1, describing them as operating together after a single implantation:

> [M] icro-coating polymer 302 [of pellet A in FIG. 3A] can be of thickness 0.2 μm and dissolve at a rate of 0.1 μm per day, thus allowing exposure to the therapeutic core 301 up to two days after **implantation**. Comparatively, micro-coating 312 [of pellet B in FIG. 3B] can have a thickness of 3.0 μm and dissolve at a rate of 0.1 μm per day, thus allowing exposure to the therapeutic core 311 up to thirty days after **implantation**. **In this example, micro**

> **coated pellet A would start releasing its content before pellet B starts. There may be a small overlap where both micro coated pellets A and B are releasing simultaneously. Finally, pellet B continues releasing its drug mixture long after pellet A has been completely dissolved.**
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> * * *
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> **[T]he pellet in FIG. 3C starts releasing its contents as pellets of FIGS. 3A and 3B near expiration.**

Specification, paras. 30, 32 (emphasis added).

Finally, the original claims, which form part of the original disclosure, stated:

> 12. **A medical device** for implantation in a body comprising:
> a bio-compatible structure; and
> **a plurality of coated pellets**, wherein each of said coated pellets comprises an active substance encapsulated by a protective layer.
>
> 13. The medical device of claim 12, wherein the plurality of coated pellets comprise at least a **first set of pellets** and a **second set of pellets**, wherein the first set of pellets has a faster decomposition rate that the second set of pellets.
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> 15. The medical device of claim 13, wherein the protective layer on the second set of pellets is **thicker** than the protective layer on the second [sic, first] set of pellets.

Original Claims 13-15. This discloses different sets of pellets on the same structure.

The Applicant respectfully submits that a person of ordinary skill in the art, reading these passages from the Abstract, Summary of Invention, Detailed Description, and Claims, would recognize that the original disclosure does disclose different sets of pellets with different coatings (thick and thin) on a single structure. Thus, for the foregoing reasons, the Applicant respectfully requests reconsideration of the rejection under 35 USC 112.

Objection to the Drawings

In the Final Office Action dated September 23, 2005, the drawings were objected to under 37 CFR 1.83(a). That Office Action stated that "the second set of pellets deposited on the structure at a second site" must be shown. Office Action dated September 23, 2005, page 3.

The Applicant respectfully submits that FIG. 1 shows a structure with four sets of pellets, labeled 130, 140, 150 and 160. The Specification specifically states that these pellets have "a **different** composition and/or dissolution (decomposition) rate." Specification, para. 18 (emphasis added). As described above, the Specification expressly states that the regions where each set of pellets is deposited can be a column or row (extending in a plane perpendicular to the drawing sheet), or the sets can be discontiguous and/or disconnected. The detailed views of FIGS. 3A-3D show examples of four pellets A-D that can correspond to the four pellets 130, 140, 150 and 160. Pellets A-D are pellets with different thicknesses. Accordingly, the Applicant respectfully submits that the current drawings do illustrate the claimed subject matter, and reconsideration of the objection to the drawings is respectfully requested.

Rejections Under 35 USC 103(a)

In the Final Office Action dated September 23, 2005, the claims were rejected under 35 USC 103(a) as being unpatentable over U.S. Patent No. 6,849,089 to Stoll (the "Stoll '089 patent"), either alone or in combination with U.S. Patent No. 6,339,130 to Bennett et al. The Applicant respectfully requests reconsideration of this rejection, for the following reasons.

First, independent claims 1, 12 and 17 recite that each of the first pellets "contain[s] a substance **in addition to** the [first] therapeutic composition [or active substance]." Claims 1, 12

and 17 (emphasis added). The Office Action of September 23, 2005, states that this limitation "can be interpreted broadly because a 'substance in addition to the first therapeutic composition' can simply be the make-up of the degradable polymer." Office Action dated September 23, 2005, page 5. By this, the rejection is apparently equating the coating of the Stoll '089 patent with the additional "substance" of the claims. However, the Applicant respectfully points out that the claims in issue separately recite a pellet "coating" or "protective layer." This coating is a **separate** element of the claims from the additional "substance" at issue. The Applicant thus respectfully submits that the claims are patentable over the Stoll '089 patent because the claims require the separate coating, therapeutic agent, and additional "substance," where the additional "substance" is a separately recited and therefore distinct element from the coating. The Stoll '089 patent discloses no additional "substance."

Second, independent claims 1, 12 and 17 recite that the pellets with different coating thicknesses have "substantially the same size" (because of the additional substance). In the Stoll '089 embodiment of Figure 7, the microcapsules have different coating thicknesses, but they have **different** sizes. The Office Action of September 23, 2005, recognizes that the Stoll '089 patent does not specify the claimed feature of pellets with different coating thicknesses but "substantially the same size," but the Office Action states that this is an obvious "design modification." However, this is not simply an obvious "design modification" but an invention that involved the conception that providing similarly-sized pellets would be advantageous **and** the conception of a specific way in which to achieve similarly-sized pellets, i.e., by providing an additional substance as claimed. The Applicant's Specification provides detailed examples of different drug/placebo mixtures that can be used to achieve similarly-sized pellets with different

coating thicknesses. The chart above summarizes some of these details. None of the cited references discloses or suggests having pellets with different thicknesses but with additional substances to achieve "substantially the same size." Accordingly, the Applicant respectfully submits that the claims are patentable over the Stoll '089 patent and the other art of record. Thus, reconsideration of the rejection under 35 USC 103(a) is respectfully requested.

CONCLUSION

Should any questions arise concerning this matter, the Examiner is invited to contact Applicant's undersigned attorney at (202) 220-4200. The Office is hereby authorized to charge any additional fees under 37 C.F.R. §1.16 or §1.17 or credit any overpayment to Deposit Account No. 11-0600.

Respectfully submitted,

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